Appl. No. 10/598,149 Amdt. dated Nov. 6, 2009

Reply to Office Action of August 6, 2009

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

- (currently amended) A truncated thrombomodulin protein derivative comprising epidermal growth factor (EGF)-like domains (4-6) EGF (4-6)-like domains, a substitution of Leucine for methionine, and a GGM amino acid motif appended at a carboxy terminus of said derivative, said <u>truncated thrombomodulin</u> protein derivative comprising SEQ ID NO:3, <u>wherein the leucine for methionine</u> substitution is at amino acid position number 40 of SEQ ID NO:3.
- (currently amended) The truncated thrombomodulin protein of claim 1 wherein said GGM protein motif is expressed as a protein motif with a non-natural amino acid corresponding to the M amino acid residue <u>at amino acid position number</u> 147 of SEQ ID NO:3.
- (currently amended) A truncated thrombomodulin protein comprising the amino acid of SEQ ID NO:3.
- 4. (currently amended) A truncated thrombomodulin derivative conjugate comprising a truncated thrombomodulin derivative and a polymer; wherein the thrombomodulin derivative comprises EGF (4-6) like domains, a substitution of Leucine for methionine, and a GGM amino acid motif appended at a carboxy terminus of said derivative, said derivative conjugate comprising SEQ ID NO:3, wherein the leucine for methionine substitution is at amino acid position number 40 of SEQ ID NO:3.
- (original) The conjugate of claim 4 wherein the polymer comprises polyethylene glycol.
- (withdrawn currently amended) A truncated thrombomodulin nucleic acid derivative comprising EGF (4-6) like domains, a substitution of Leucine for methionine at position 388, and a nucleic acid sequence capable of encoding a

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- Gly Gly Met motif appended at a carboxy terminus of said derivative, <u>wherein</u> said <u>nucleic acid encodes the truncated thrombomodulin protein amino acid</u> sequence of claim 3.
- (withdrawn) The thrombomodulin nucleic acid derivative of claim 6 comprising SEQ ID NO:1.
- 8. (withdrawn currently amended) A method of generating a purified truncated thrombomodulin derivative protein, wherein the protein comprises EGF (4-6) like domains, a substitution of Leucine for methionine at position 388, and a non-natural amino acid; comprising the steps of providing a truncated thrombomodulin nucleic acid sequence; recombinantly expressing said nucleic acid sequence in the presence of a non-natural amino acid precursor; and purifying a recombinant expression product; thereby generating a purified truncated thrombomodulin derivative protein, wherein the recombinant expression product comprises the amino acid sequence the truncated thrombomodulin protein of claim 3.
- (withdrawn) The method of claim 8 wherein said nucleic acid sequence is SEQ ID NO:1
- 10. (withdrawn) The method of claim 8 wherein the non-natural amino acid is selected from the group consisting of: methionine analogues, alanine analogues, phenylalanine analogues, leucine analogues, proline analogues and isoleucine analogues.
- (withdrawn) The method of claim 10 wherein said methionine analog is L-2amino-4-azido-butanoic acid.
- (withdrawn) The method of claim 8 wherein the non-natural amino acid is located at a C-terminal portion of the construct.
- (withdrawn) A method of site-specific PEGylation of a bioactive protein, comprising identifying an amino acid residue capable of alteration wherein the

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alteration does not substantially impair a protein activity; altering said amino acid residue; integrating a non-natural amino acid residue into said bioactive protein at a site, and conjugating a PEG polymer to said non-natural amino acid at the site.

- (withdrawn) The method of claim 13 wherein the bioactive protein is thrombomodulin.
- (withdrawn) The method of claim 13 wherein the bioactive protein is a thrombomodulin derivative.
- (currently amended) A conjugate of a truncated thrombomodulin protein derivative-polymer conjugate thrombomodulin protein or a thrombomodulin derivative and a polymer, wherein said truncated thrombomodulin protein derivative conjugate comprises SEQ ID NO:3.
- (currently amended) The conjugate of claim 16 wherein the polymer is polyethylene glycol PEG.
- 18. (original) The conjugate of claim 16 wherein the polymer can confer a property for the conjugate selected from the group consisting of: an increase in plasma half-life, stability against proteolytic cleavage, and a decrease of protein immunogenicity, or combination thereof.
- 19. (original) The conjugate of claim 16 wherein the conjugate is soluble.
- (currently amended) A <u>truncated</u> thrombomodulin <u>protein</u> derivative comprising a eatalytically <u>catalytic</u> active site capable of activating protein C and a non-natural amino acid, said <u>truncated thrombomodulin protein</u> derivative comprising SEQ ID NO:3 and <u>said non-natural amino acid is at the C-terminal portion of SEQ ID</u> NO:3.

Claims 21-22 (canceled)

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- (currently amended) The <u>truncated</u> thrombomodulin <u>protein</u> derivative of claim 20 conjugated via said non-natural amino acid to a linear or branched natural or synthetic polymer.
- 24. (currently amended) The derivative of claim 23 wherein said linear or branched synthetic polymer is selected from the group consisting of poly(t-butyl acrylate), poly(t-butyl methacrylate), polyacrylamide, glycolipid, and their mimeties; and other polymers; glycoproteins and their mimeties, poly(arginine), and polysaccharides and their mimeties; and other polymers as would be understood in the art.

Claims 25-60 (canceled)